

**Amendment of the claims:**

Please amend claims 1, 20 and 25 as set forth below. Please add new claims 28-31.

The present listing of the claims replaces any prior listing and upon entry of the present amendment, the status of the claims will be as follows:

**Listing of the claims:**

1. (Currently amended) A method for detecting the presence of a mammalian mutant target nucleic acid ~~which contributes to the etiology of a~~ in a neoplasm ~~[[,]]~~ and in a tumor margin tissue specimen comprising,

~~wherein the specimen is external to a primary neoplasm and the specimen does not exhibit morphological characteristics indicative of neoplastic pathology, and.~~

~~the mutant target nucleic acid is present in the primary neoplasm and the specimen, the method comprising extracting the mutant nucleic acid present in the neoplasm and in the tissue specimen and detecting the presence of the mutant target nucleic acid, wherein the mutant target nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1; and~~

detecting the mutant target nucleic acid in the neoplasm and in the tissue specimen, wherein the specimen is external to a primary neoplasm and the specimen does not exhibit microscopic characteristics indicative of neoplastic pathology.

2. (Previously presented) The method of claim 1, further comprising, prior to detecting the presence of the mutant target nucleic acid, amplifying the nucleic acid present in the specimen to produce an amplified nucleic acid, wherein said detecting comprises detecting the presence of the mutant target nucleic acid in the amplified nucleic acid.

3. (Previously presented) The method of claim 2, wherein said amplifying is by means of oligonucleotides that hybridize to flanking regions of the mutant target nucleic acid.

4. (Previously presented) The method of claim 1, wherein the mutant target nucleic acid contains a mutation selected from the group consisting of a restriction fragment length polymorphism, a nucleic acid deletion, and a nucleic acid substitution.

5 and 6. (Cancelled)

7. (Previously presented) The method of claim 1, wherein the neoplasm is a neoplasm of the head or a neoplasm of the neck.

8. (Previously presented) The method of claim 1, wherein the neoplasm is head and neck cancer.

9. (Previously presented) The method of claim 1, wherein the neoplasm is a benign neoplasm.

10. (Previously presented) The method of claim 1, wherein the neoplasm is a malignant neoplasm.

11. (Previously presented) The method of claim 2, further comprising, prior to detecting the presence of the mutant nucleic acid, cloning the amplified nucleic acid, wherein said detecting comprises detecting the presence of the mutant target nucleic acid in the amplified nucleic acid.

12. (Previously presented) A method for detecting metastases in a subject having an excised tumor, the method comprising:

- a) isolating tissue from a surgical margin adjacent to the excised tumor;
- b) applying to said tissue an oligonucleotide that specifically hybridizes to a neoplastic nucleic acid having a mutant nucleotide sequence, wherein the neoplastic nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1; and
- c) detecting the presence of said neoplastic nucleic acid, wherein the presence of said neoplastic nucleic acid indicates metastases.

13. (Original) The method according to claim 12 wherein no more than an average of about one out of every ten thousand cells of said tissue have a neoplastic nucleic acid.

14. (Original) The method according to claim 12 wherein said tissue appears normal under a microscope.

15 to 17. (Cancelled)

18. (Previously presented) A method for detecting a mammalian target neoplastic nucleic acid having a mutant nucleotide sequence in a tissue specimen which is external to a primary neoplasm, comprising extracting nucleic acid present in the specimen to obtain extracted nucleic acid, and detecting the presence of the target neoplastic nucleic acid in the extracted nucleic acid, wherein the target neoplastic nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1.

19. (Previously presented) A method for detecting a mammalian target neoplastic nucleic acid having a mutant nucleotide sequence in a tumor margin tissue specimen which is external to a primary neoplasm, comprising extracting nucleic acid present in the specimen to

obtain extracted nucleic acid, and detecting the presence of the target neoplastic nucleic acid in the extracted nucleic acid, wherein the target neoplastic nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1.

20. (Currently amended) A method for detecting the presence of a mammalian mutant target nucleic acid ~~which contributes to the etiology of a neoplasm, in a neoplasm and in a lymph node tissue specimen, comprising:~~

~~wherein the specimen is external to a primary neoplasm and the specimen does not exhibit morphological characteristics indicative of neoplastic pathology, and~~

~~the mutant target nucleic acid is present in the primary neoplasm and the specimen, the method comprising extracting mutant nucleic acid present in the neoplasm and in the tissue specimen and detecting the presence of the mutant target nucleic acid, wherein the mutant target nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1; and~~

~~detecting the mutant target nucleic acid in the neoplasm and in the tissue specimen, wherein the specimen is external to a primary neoplasm and the specimen does not exhibit microscopic characteristics indicative of neoplastic pathology.~~

21. (Previously presented) The method of claim 20, further comprising, prior to detecting the presence of the mutant target nucleic acid, amplifying the nucleic acid present in the specimen to produce an amplified nucleic acid, wherein said detecting comprises detecting the presence of the mutant target nucleic acid in the amplified nucleic acid.

22. (Previously presented) The method of claim 20, wherein the mutant target nucleic acid contains a mutation selected from the group consisting of a restriction fragment length polymorphism, a nucleic acid deletion, and a nucleic acid substitution.

23. (Canceled)

24. (Previously presented) The method of claim 20, wherein the neoplasm is a neoplasm of the head or a neoplasm of the neck.

25. (Currently amended) A method for detecting metastases in a subject having an excised tumor, the method comprising:

a) isolating tissue from a lymph node, which is external to a primary neoplasm and does not exhibit ~~morphological~~ microscopic characteristics indicative of neoplastic pathology;

b) applying to said tissue an oligonucleotide that specifically hybridizes to a neoplastic nucleic acid having a mutant nucleotide sequence, wherein the neoplastic nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1; and

c) detecting the presence of said neoplastic nucleic acid, wherein the presence of said neoplastic nucleic acid indicates metastases.

26. (Previously presented) The method of claim 25, wherein no more than an average of about one out of every ten thousand cells of said tissue have a neoplastic nucleic acid.

27. (Canceled)

28. (New) A method for detecting the presence of a mammalian mutant target nucleic acid in a neoplasm and in a tumor margin tissue specimen comprising,

extracting the mutant nucleic acid present in the neoplasm and in the tissue specimen;

detecting the mutant target nucleic acid in the neoplasm and in the tissue specimen,

wherein the specimen is external to a primary neoplasm and the specimen does not exhibit microscopic characteristics indicative of neoplastic pathology; and

detecting the presence of the nucleic acid in the neoplasm, wherein the presence of the nucleic acid in the neoplasm indicates tumor extension or metastases.

29. (New) A method for detecting metastases in a subject having an excised tumor, the method comprising:

- a) isolating tissue from a surgical margin adjacent to the excised tumor, wherein the surgical margin does not exhibit microscopic characteristics indicative of neoplastic pathology;
- b) applying to said tissue an oligonucleotide that specifically hybridizes to a neoplastic nucleic acid having a mutant nucleotide sequence; and
- c) detecting the presence of said neoplastic nucleic acid, wherein the presence of said neoplastic nucleic acid indicates tumor extension or metastases.

30. (New) A method for detecting a mammalian target neoplastic nucleic acid having a mutant nucleotide sequence in a tissue specimen which is external to a primary neoplasm, comprising extracting nucleic acid present in the specimen to obtain extracted nucleic acid, wherein the specimen does not exhibit microscopic characteristics indicative of neoplastic pathology, and detecting the presence of the target neoplastic nucleic acid in the extracted nucleic acid.

31. (New) A method for detecting the presence of a mammalian mutant target nucleic acid in a neoplasm and in a lymph node tissue specimen, comprising:

- extracting mutant nucleic acid present in the neoplasm and in the tissue specimen; and
  - detecting the mutant target nucleic acid in the neoplasm and in the tissue specimen,
- wherein the specimen is external to a primary neoplasm and the specimen does not exhibit microscopic characteristics indicative of neoplastic pathology.